UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

Note to Reader
September 9, 1998

Background: As part of its effort to involve the public in the implementation of the Food Quality Protection Act of 1996 (FQPA), which is designed to ensure that the United States continues to have the safest and most abundant food supply, EPA is undertaking an effort to open public dockets on the organophosphate pesticides. These dockets will make available to all interested parties documents that were developed as part of the U.S. Environmental Protection Agency's process for making reregistration eligibility decisions and tolerance reassessments consistent with FQPA. The dockets include preliminary health assessments and, where available, ecological risk assessments conducted by EPA, rebuttals or corrections to the risk assessments submitted by chemical registrants, and the Agency's response to the registrants' submissions.

The analyses contained in this docket are preliminary in nature and represent the information available to EPA at the time they were prepared. Additional information may have been submitted to EPA which has not yet been incorporated into these analyses, and registrants or others may be developing relevant information. It's common and appropriate that new information and analyses will be used to revise and refine the evaluations contained in these dockets to make them more comprehensive and realistic. The Agency cautions against premature conclusions based on these preliminary assessments and against any use of information contained in these documents out of their full context. Throughout this process, if unacceptable risks are identified, EPA will act to reduce or eliminate the risks.

There is a 60 day comment period in which the public and all interested parties are invited to submit comments on the information in this docket. Comments should directly relate to this organophosphate and to the information and issues

available in the information in this docket. Once the comment period closes, EPA will review all comments and revise the risk assessments, as necessary.

These preliminary risk assessments represent an early stage in the process by which EPA is evaluating the regulatory requirements applicable to existing pesticides. Through this opportunity for notice and comment, the Agency hopes to advance the openness and scientific soundness underpinning its decisions. This process is designed to assure that America continues to enjoy the safest and most abundant food supply. Through implementation of EPA's tolerance reassessment program under the Food Quality Protection Act, the food supply will become even safer. Leading health experts recommend that all people eat a wide variety of foods, including at least five servings of fruits and vegetables a day.

Note: This sheet is provided to help the reader understand how refined and developed the pesticide file is as of the date prepared, what if any changes have occurred recently, and what new information, if any, is expected to be included in the analysis before decisions are made. **It is not meant to be a summary of all current information regarding the chemical.** Rather, the sheet provides some context to better understand the substantive material in the docket (RED chapters, registrant rebuttals, Agency responses to rebuttals, etc.) for this pesticide.

Further, in some cases, differences may be noted between the RED chapters and the Agency's comprehensive reports on the hazard identification information and safety factors for all organophosphates. In these cases, information in the comprehensive reports is the most current and will, barring the submission of more data that the Agency finds useful, be used in the risk assessments.

Jack Housenger, Acting Director
Special Review and Reregistration
Division

4/29/98

MEMORANDUM

SUBJECT: Fenthion HED RED Chapter. Update to Incorporate FQPA Considerations. P.C.Code 053301. Case No. 0290. DP Barcode D245312.

FROM: William J. Hazel, Ph.D.
Reregistration Branch 1
Health Effects Division (7509C)

THRU: Whang Phang, Ph.D., Branch Senior Scientist
Reregistration Branch 1
Health Effects Division (7509C)

TO: Dennis Deziel/Arnold Layne (PM 51)
Reregistration Branch 1
Special Review and Reregistration Division (7508W)

This memorandum and attachments serve to revise and update the HED RED Chapter for Fenthion (J. Smith, 5/31/96) by addressing considerations necessitated by the 1996 Food Quality Protection Act (FQPA). Attachments include the greatly revised draft HED RED Chapter by W. Hazel dated 4/16/98 (Attachment 1), the most recent HED Hazard Identification Assessment Review Committee (HIARC) report by J. Rowland dated 3/26/98 (Attachment 2), Occupational/ Residential aspects of the RED (text is incorporated into Attachment 1) by J. Dawson dated 4/2/98 (Attachment 3), and the 9/23/97 Acute and Chronic Dietary Risk Assessments (Attachment 4).

Fenthion is an organophosphate insecticide. Cumulative risk assessment considering risks from other pesticides having a common mechanism of toxicity is not addressed in this document.

Fenthion is formulated as soluble concentrates, ready-to-use products, and impregnated material (ear tag) for livestock direct animal treatments and wide area mosquito (adulticide) control. There is some indication from REFS that three granular products are registered for wide area mosquito (larvicide) control; as mosquito larvae are aquatic, this strongly implies application to

water. While HED did estimate occupational exposures reflecting application of these granular products, it does not appear as though water residue estimates reflected this use pattern. There are no residential uses of fenthion although there is residential exposure resulting from the mosquito abatement use.

Technical fenthion is classified as Toxicity Category II for oral, dermal, and inhalation toxicity, Category III for eye irritation, and Category IV for dermal irritation. Cholinesterase inhibition, with or without attendant cholinergic signs, were the principal toxic effects associated with all risk assessment endpoints. Doses and endpoints for all exposure scenarios except inhalation were derived from an oral 2-year monkey study and/or a 28-day human oral dosing study often supported by rabbit and rodent studies. Recently submitted acute and subchronic neurotoxicity studies (rat) have satisfied earlier deficiencies and have, in conjunction with developmental toxicity studies, obviated the need for a developmental neurotoxicity study. Also based on the new developmental and neurotoxicity studies, HED's Hazard Identification Assessment Review Committee (HIARC) has recommended that the 10x FQPA uncertainty factor for infants and children be removed; the final decision will soon be made by HED's FQPA Safety Committee taking hazard **and** exposure considerations into account. There was no evidence of carcinogenicity in any fenthion study. A new dominant lethal mutagenicity study is required to confirm the negative results of an older study. A subchronic inhalation toxicity study is tentatively required to assess the effects of repeated inhalation exposure; use pattern considerations and relative contribution of inhalation exposure, compared to dermal exposure, to the total daily dose **may** negate the need for this study.

Significant occupational exposure to fenthion is expected based on surrogate exposure estimates using the Pesticide Handler Exposure Database (PHED). Dermal and inhalation MOEs were combined because inhalation risks were quite small compared to those associated with the dermal route of exposure. For short and intermediate dermal risk assessment, the doses used were 0.07 and 0.02 mg/kg/day, respectively, from the 28-day human oral study in which plasma cholinesterase inhibition was the endpoint (threshold NOEL/LOEL was 0.02 mg/kg/day). Dermal absorption was assumed to be 20% based on a comparison of rabbit oral and dermal toxicity studies. The LOEL of 0.209 mg/L (36.34 mg/kg/day) was used for inhalation risk assessment based on a 4-hour rat study in which cholinergic signs and mortality were observed. Calculation of combined dermal and inhalation risks resulted in short-term MOEs of <6 for occupational scenarios involving mixing/loading and applying liquids aerially even after application of engineering controls (closed mixing or closed cockpit); short-term risks were considered adequately protective (MOE >10) for other exposure scenarios utilizing engineering controls. Intermediate-term risks to all occupational scenarios using engineering controls were unacceptable (MOEs of 1-29 when 30 is considered protective) except in the case of the granular loading scenario for aerial applications which was acceptable using engineering controls.

In order to refine dietary exposure, anticipated residue data were generated; because all crop uses of fenthion and use on poultry are not being supported, these anticipated residues represent only milk and tissues of cattle and swine. In the case of fenthion, the magnitude of the residue data do

not represent the label directions for direct animal treatments in terms of application rate or preslaughter interval. As a result, data from the existing feeding studies were extrapolated to reflect current label directions to estimate upper bound residues in milk and cattle tissues. It was assumed that 100% of livestock are treated. The same upper bound residue estimates were used for both acute and chronic dietary risk assessments. In the case of all cattle tissues, these residues represented an increase over the current tolerance levels.

There is an acute dietary risk concern for fenthion. The endpoint used for acute dietary risk assessment was plasma cholinesterase inhibition observed at the 24-hour interval in the 28-day human oral dosing study; the dose used for risk asssessment was 0.07 mg/kg/day. MOEs from an acute DRES run, conducted 9/23/97, were 4.7 for non-nursing infants (<1 year) and children (1-6 years) and 7 for the general U.S. population and males and females (13 plus). An MOE of 10 is considered protective for acute dietary risk assessments (pending consideration by HED's FQPA Safety Committee).

A chronic DRES run was conducted 9/23/97. The RfD of 0.0007 mg/kg/day was used for risk calculations; this is based on an uncertainty factor of 30 and a LOEL of 0.02 mg/kg/day for the threshold effect of plasma cholinesterase inhibition observed in the 28-day human oral dosing study supported by the 2-year oral monkey study. Again, HED's FQPA Safety Committee will render the final decision as to the necessity of the extra 10x UF for infants and children, which the current assessment **does not** take into account. Chronic dietary risks using the anticipated residue exposure estimates were unacceptable for all population subgroups except nursing infants (<1 year). The chronic risks were generally 150-250% of the RfD; we will specifically note the following: U.S. population (209%), non-nursing infants <1 year (201%), children 1-6 years (387%), and children 7-12 years (300%). As the anticipated livestock residue levels are quite conservative (yet not refinable at this time), we expect that the required livestock magnitude of the residue studies will permit refinement and a much higher level of confidence in the database.

Although there are no homeowner uses, residential exposure assessments were conducted to permit risk calculations reflecting the use of fenthion as a residential wide area mosquito adulticide. The AgDRIFT model was used to estimate deposition of residues following aerial and ULV applications whereas published studies were used to calculate residue deposition following ground-applied ULV treatments. The Residential SOPs were used to calculate dermal exposures and subsequent risks associated therefrom. Short-term residential risks to toddlers and adults were acceptable (MOE >10) on the day of treatment: MOEs were >11 following aerial ULV and >90 reflecting ground-based ULV applications. Short-term risks declined thereafter (MOEs increasing with time, reaching >500 by day 30). In the case of intermediate-term risk, residential MOEs were 80-300, i.e., above the protective level of 30 following ground ULV applications. Residential exposure to aerial ULV applications (typical rates) resulted in acceptable risk (MOE of 38) to adults; risks to toddlers (exposed to typical or maximum rates) and adults (maximum rate only) were unacceptable (MOEs of 10-20) reflecting aerial ULV mosquito abatement treatments.

The FQPA requirement to assess the potential for increased sensitivity of infants and children has been addressed, from the hazard perspective only, by the HIARC (see Attachment 2). To assure that a consistent approach is used for all members of the organophosphates class of chemicals, HED's FQPA Safety Committee will revisit fenthion and all other members of this class later in the risk assessment/risk management process to determine, based on hazard **and** exposure aspects, the necessity and magnitude of any extra uncertainty factor to be applied to infants and children.

Aggregate exposure to fenthion will not be calculated at this time. GENEEC model estimates of fenthion water concentrations are available but we are not aware of water monitoring data. There is no residential use of fenthion although residential exposure to fenthion as a result of mosquito abatement programs is expected to result in unaccaptable intermediate-term risks as noted above.

HED notes that EFED may wish to consider the use of the AgDRIFT model to estimate fenthion deposition, and subsequent potential water concentrations, resulting from aerial ULV mosquito adulticide applications. Also, we note that REFS states that three granular products (EPA Reg. Nos. 5481-83, 5481-84, and 5481-101) are used for mosquito larva control, thus implying that aquatic uses exist. Such use patterns were only assessed from the occupational exposure perspective to our knowledge.

Attachments:

Attachment 1: HED Draft RED Chapter. W. Hazel. 4/16/98.
Attachment 2: HED HIARC report. J. Rowland. 3/26/98.
Attachment 3: Occupational/Residential RED Aspects. J. Dawson. 4/2/98. (Cover memo only).
Attachment 4: Acute and chronic DRES runs. HED. 9/23/97.

cc (with attachments): W. Hazel (RRB-1)

cc (without attachments): EFED, LAN files